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3 <110> APPLICANT: YUI, MASAKI YOKOZAWA, AKIRA ENTERED 5 MURATA, TOMOYO TSURUTA, KAZUHISA 7 SHIMIZU, HIROTOMO 9 <120> TITLE OF INVENTION: METHOD FOR KEEPING THE QUALITY OF AQUEOUS PARENTERAL SOLUTION OF THROMBOMODULIN IN STORAGE AND DISTRIBUTION 12 <130> FILE REFERENCE: KP-8753 14 <140> CURRENT APPLICATION NUMBER: 09/509,994 15 <141> CURRENT FILING DATE: 2000-05-08 17 <150> PRIOR APPLICATION NUMBER: PCT/JP98/04609 18 <151> PRIOR FILING DATE: 1998-10-13 20 <150> PRIOR APPLICATION NUMBER: JP 9-281659 21 <151> PRIOR FILING DATE: 1997-10-15 23 <150> PRIOR APPLICATION NUMBER: JP 9-308523 24 <151> PRIOR FILING DATE: 1997-11-11 26 <160> NUMBER OF SEQ ID NOS: 6 28 <170> SOFTWARE: PatentIn Ver. 2.1 30 <210> SEO ID NO: 1 31 <211> LENGTH: 516 32 <212> TYPE: PRT 33 <213> ORGANISM: Homo sapiens 35 <220> FEATURE: 36 <223> OTHER INFORMATION: Partial amino acid sequences of a human 37 thrombomodulin 39 <400> SEQUENCE: 1 40 Met Leu Gly Val Leu Val Leu Gly Ala Leu Ala Leu Ala Gly Leu Gly 41 1 43 Phe Pro Ala Pro Ala Glu Pro Gln Pro Gly Gly Ser Gln Cys Val Glu 25 46 His Asp Cys Phe Ala Leu Tyr Pro Gly Pro Ala Thr Phe Leu Asn Ala 47 35 40 49 Ser Gln Ile Cys Asp Gly Leu Arg Gly His Leu Met Thr Val Arg Ser 50 55 52 Ser Val Ala Ala Asp Val Ile Ser Leu Leu Leu Asn Gly Asp Gly Gly 70 75 55 Val Gly Arg Arg Arg Leu Trp Ile Gly Leu Gln Leu Pro Pro Gly Cys 85 58 Gly Asp Pro Lys Arg Leu Gly Pro Leu Arg Gly Phe Gln Trp Val Thr 105 61 Gly Asp Asn Asn Thr Ser Tyr Ser Arg Trp Ala Arg Leu Asp Leu Asn 115 120 64 Gly Ala Pro Leu Cys Gly Pro Leu Cys Val Ala Val Ser Ala Ala Glu 130 135 140 67 Ala Thr Val Pro Ser Glu Pro Ile Trp Glu Glu Gln Gln Cys Glu Val 150 155

70 Lys Ala Asp Gly Phe Leu Cys Glu Phe His Phe Pro Ala Thr Cys Arg

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170

73 Pro Leu Ala Val Glu Pro Gly Ala Ala Ala Ala Ala Val Ser Ile Thr 180 185 76 Tyr Gly Thr Pro Phe Ala Ala Arg Gly Ala Asp Phe Gln Ala Leu Pro 77 195 200 205 79 Val Gly Ser Ser Ala Ala Val Ala Pro Leu Gly Leu Gln Leu Met Cys 215 82 Thr Ala Pro Pro Gly Ala Val Gln Gly His Trp Ala Arg Glu Ala Pro 230 85 Gly Ala Trp Asp Cys Ser Val Glu Asn Gly Gly Cys Glu His Ala Cys 245 250 88 Asn Ala Ile Pro Gly Ala Pro Arg Cys Gln Cys Pro Ala Gly Ala Ala 265 91 Leu Gln Ala Asp Gly Arg Ser Cys Thr Ala Ser Ala Thr Gln Ser Cys 92 275 280 94 Asn Asp Leu Cys Glu His Phe Cys Val Pro Asn Pro Asp Gln Pro Gly 95 290 295 300 97 Ser Tyr Ser Cys Met Cys Glu Thr Gly Tyr Arg Leu Ala Ala Asp Gln 310 315 100 His Arg Cys Glu Asp Val Asp Asp Cys Ile Leu Glu Pro Ser Pro Cys 330 325 103 Pro Gln Arg Cys Val Asn Thr Gln Gly Gly Phe Glu Cys His Cys Tyr 340 345 106 Pro Asn Tyr Asp Leu Val Asp Gly Glu Cys Val Glu Pro Val Asp Pro 107 355 360 365 109 Cys Phe Arg Ala Asn Cys Glu Tyr Gln Cys Gln Pro Leu Asn Gln Thr 375 380 112 Ser Tyr Leu Cys Val Cys Ala Glu Gly Phe Ala Pro Ile Pro His Glu 390 395 115 Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp 405 410 118 Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile 425 121 Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly 122 435 440 445 124 Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys 125 450 455 460 127 Ile Cys Gly Pro Asp Ser Ala Leu Val Arg His Ile Gly Thr Asp Cys 470 475 130 Asp Ser Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro 485 490 133 Pro Ser Pro Thr Pro Gly Ser Thr Leu Thr Pro Pro Ala Val Gly Leu 500 505 136 Val His Ser Glv 137 515 140 <210> SEO ID NO: 2 141 <211> LENGTH: 516 142 <212> TYPE: PRT

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153	Phe	Pro	Ala	Pro	Ala	Glu	Pro	Gln	Pro	Gly	Gly	Ser	Gln	Cys	Val	Glu
154				20					25					30		
156	His	Asp	Cys	Phe	Ala	Leu	Tyr	Pro	Gly	Pro	Ala	Thr	Phe	Leu	Asn	Ala
157			35					40					45			
159	Ser	Gln	Ile	Cys	Asp	Gly	Leu	Arg	Gly	His	Leu	Met	Thr	Val	Arg	Ser
160		50					55					60				
162	Ser	Val	Ala	Ala	Asp	Val	Ile	Ser	Leu	Leu	Leu	Asn	Gly	Asp	Gly	Gly
163	65					70					75					80
165	Val	Gly	Arg	Arg	Arg	Leu	Trp	Ile	Gly	Leu	Gln	Leu	Pro	Pro	Gly	Cys
166			-	-	85					90					95	
168	Glv	Asp	Pro	Lys	Arq	Leu	Gly	Pro	Leu	Arg	Gly	Phe	Gln	Trp	Val	Thr
169		•		100	-		•		105					110		
171	Glv	Asp	Asn	Asn	Thr	Ser	Tyr	Ser	Arq	Trp	A1a	Arg	Leu	Asp	Leu	Asn
172			115				•	120	-	-			125	_		
174	Glv	Ala	Pro	Leu	Cvs	Glv	Pro	Leu	Cys	Val	Ala	Val	Ser	Ala	Ala	Glu
175		130			-	-	135		•			140				
177	Ala	Thr	Val	Pro	Ser	Glu	Pro	Ile	Trp	Glu	Glu	Gln	Gln	Cys	Glu	Val
178	145					150					155					160
		Ala	Asp	Glv	Phe	Leu	Cvs	Glu	Phe	His	Phe	Pro	Ala	Thr	Cvs	Arq
181	-1-				165					170					175	-
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184				180			2		185					190		
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187	-2-		195					200	-				205			
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190		210					215				-	220				-
	Thr		Pro	Pro	Glv	Ala	Val	Gln	Glv	His	Trp	Ala	Arq	Glu	Ala	Pro
	225				1	230					235		-			240
		Ala	Trp	Asp	Cvs		Val	Glu	Asn	Glv	Glv	Cvs	Glu	His	Ala	Cys
196					245					250	-	-			255	•
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	Pro	a en	Tyr		Len	Va 1	Agn	Glv		Cvs	Va 1	Glu	Pro		Asp	Pro
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                                            395
225 Pro His Arg Cys Gln Met Phe Cys Asn Gln Thr Ala Cys Pro Ala Asp
226
                    405
                                        410
228 Cys Asp Pro Asn Thr Gln Ala Ser Cys Glu Cys Pro Glu Gly Tyr Ile
                                                        430
229
                420
                                    425
231 Leu Asp Asp Gly Phe Ile Cys Thr Asp Ile Asp Glu Cys Glu Asn Gly
                                                    445
            435
                                440
234 Gly Phe Cys Ser Gly Val Cys His Asn Leu Pro Gly Thr Phe Glu Cys
        450
                            455
237 Ile Cys Gly Pro Asp Ser Ala Leu Ala Arg His Ile Gly Thr Asp Cys
238 465
                        470
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240 Asp Ser Gly Lys Val Asp Gly Gly Asp Ser Gly Ser Gly Glu Pro Pro
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262 ggccccgcga ccttcctcaa tgccagtcag atctgcgacg gactgcgggg ccacctaatg 180
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267 tecgetgetg aggecactgt geeeagegag eegatetggg aggageagea gtgegaagtg 480
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274 acceptatecy cyacycayte etgeaacyae etetgegage aettetgegt teccaaecee 900
275 gaccagecgg getectaete gtgeatgtge gagacegget aceggetgge ggeegaecaa 960
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- peptide
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